Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	564	"bone marrow" with aspirate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 14:58
L2	39	l1 SAME (heparin or anticoagulant)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 14:58
L3	0	l2 SAME hypoxia	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 14:58
L4	0	l2 SAME "low oxygen"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 14:58
L5	31726	low near3 oxygen	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 14:58
L6	75	hypox$ and l1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 14:59
L7	5	l2 and l6	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:01
L8	0	l2 and l5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 14:59
L9	17562	"GM-CSF" or MCP-1 or EPAS or HIF	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:02
L10	1	l7 and l9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:08
L11	47	kornowski.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:08
L12	7	l11 and "autologous bone marrow"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:23

L13	35	PAEC and "bone marrow"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:26
L14	0	PAEC and ("bone marrow" SAme aspirate)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:27
L15	6	"5610056".pn. or "5997860".pn. or "20050032600"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:40
L16	4	"5610056".pn. or "5997860".pn. or "20050032600A1"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:40
L17	0	"2005/0032600A1"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:40
L18	0	"2005/0032600 A1"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 15:40
L19	2	mickle.in. and "bone marrow"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 16:05
L20	30	"6127525"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 16:39
L21	694	MC-1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 16:39
L22	1303	"monocyte chemoattractant protein"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 16:55
L23	0	l22 and l2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 16:55
L24	0	l22 and l6	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 16:55

L25	0	l22 and l6	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 16:55
L26	5	l22 and l1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 16:56
L27	184577	bone marrow or autologous bone marrow	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L28	3577	(bone marrow or autologous bone marrow) SAME myocardial	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L31	8	RGTA	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L32	2888	"cell therapy"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L35	39159	"bone marrow"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L52	24	chiu.in. and "bone marrow"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L55	12	cytokine SAME angio	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L56	23407	cytokine SAME stimulat$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L58	97	((("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)) and aspirate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L59	13	((((("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)) and aspirate) and MCP	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27

L60	55768	heparin or anticoagulant	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L61	42	((((("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)) and aspirate) and (heparin or anticoagulant)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L62	12	(((((("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)) and aspirate) and MCP) and (heparin or anticoagulant)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L63	70	IL-3 WITH angiogen$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L64	74	(IL-3 or IL3) WITH angiogen$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L69	1	"5997860".pn. and "bone marrow"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L70	2	"5610056".pn. and bone	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L106	31	fuchs and "autologous bone marrow"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L107	4	("cell therapy" same "bone marrow") same transfection	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L108	17	("bone marrow" same (transfection of "genetic modification")) same (angiogenic or angiogenesis or neovascularization or "myocardial contractility")	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L109	16	("early attaching cells" or "adhering cells") same (transfection or "genetic modification" or "gene transfer")	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L110	5	(("bone marrow" or "autologous bone marrow") SAME transfection) SAME confluent	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27

L111	45	(("bone marrow" or "autologous bone marrow") SAME attach) and transfection	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L112	74	(("bone marrow" or "autologous bone marrow") SAME attach) and (transfection or transduction)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L113	24	chiu.in. and "bone marrow"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L114	12	cytokine SAME angio	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/28 17:27
L128	2308	marrow SAME cytokine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L129	2119	L128 and stimulat$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L130	184577	bone marrow or autologous bone marrow	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L131	3577	(bone marrow or autologous bone marrow) SAME myocardial	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L182	2308	marrow SAME cytokine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27
L183	2119	L182 and stimulat$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/09/28 17:27

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     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 16:58:36 ON 28 SEP 2005
L1         57352 S KORNOWSKI?/AU OR MICKLE?/AU OR FUCHS?/AU OR EPSTEIN?/AU
L2         15603 S "AUTOLOGOUS BONE MARROW"
L3          8313 S "BONE MARROW" (2W) ASPIRAT?
L4         16808 S "MONOCYTE CHEMOATTRACTANT PROTEIN" OR MCP-1
L5            36 S HYPOX? AND L2
L6            31 S L5 NOT PY>=2000
L7            16 DUP REM L6 (15 DUPLICATES REMOVED)
L8             0 S L7 AND L3
L9         53677 S HIF1 OR HIF-1 OR EPAS OR MCP1 OR MCP-1 OR GMCSF OR GM-CSF
L10       111142 S ANGIOGENESIS OR ARTERIOGENESIS OR NEOVASCULARIZATION OR (COLL
L11            8 S L1 AND L2 AND L9
L12            5 DUP REM L11 (3 DUPLICATES REMOVED)
L13            2 S L12 NOT PY>=2000
L14            0 S L2 AND L3 AND L4
L15            4 S L3 AND L4
L16            0 S L15 NOT PY>=2000
L17            3 DUP REM L15 (1 DUPLICATE REMOVED)
L18            0 S L3 AND (CULTURE (P) HYPOXIA)
L19            4 S L3 AND L4
L20           31 S L5 NOT PY>=2000
L21           16 DUP REM L20 (15 DUPLICATES REMOVED)
L22           16 DUP REM L20 (15 DUPLICATES REMOVED)
L23            0 S L22 AND L10
L24            1 S L22 AND L9
L25          170 S L10 AND L2
L26            1 S L25 AND ASPIRATE
L27            3 S L25 AND HYPOX?
L28            3 DUP REM L27 (0 DUPLICATES REMOVED)
L29           73 S L3 AND L9
L30            4 S L3 AND L4
L31           37 S L29 NOT PY>=2000
L32            0 S L30 NOT PY>=2000
L33           14 DUP REM L31 (23 DUPLICATES REMOVED)

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L13 ANSWER 2 OF 2 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 89069230 EMBASE
DOCUMENT NUMBER: 1989069230
TITLE: In vivo administration of recombinant human granulocyte/macrophage colony-stimulating factor in acute lymphoblastic leukemia patients receiving purged autografts.
AUTHOR: Blazar B.R.; Kersey J.H.; McGlave P.B.; Vallera D.A.; Lasky L.C.; Haake R.J.; Bostrom B.; Weisdorf D.R.; **Epstein C.**; Ramsay N.K.C.
CORPORATE SOURCE: UMHC, University of Minnesota, Minneapolis, MN 55455, United States
SOURCE: Blood, (1989) Vol. 73, No. 3, pp. 849-857.
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911212
Last Updated on STN: 911212

AB Based on the recent reports that recombinant human granulocyte/macrophage colony-stimulating factor (rhGM-CSF) accelerates the rate of engraftment in a variety of **autologous bone marrow** transplantation settings, we have investigated its effects on hematopoietic recovery of patients with acute lymphoblastic leukemia (ALL) undergoing **autologous bone marrow** transplantation. Our studies, which involved 25 autologous ALL recipients who received rhGM-CSF and 27 controls similar for disease status (remission or relapse) and disease type (B- or T-lineage) differed from previous studies in one important aspect: the bone marrows were purged with 4-hydroperoxycyclophosphamide (4HC) and anti-T or anti-B-cell lineage-specific antibodies before transplantation. Such treatments frequently lead to a reduction in the CFU-GM content of the transplanted marrow. Eighteen of 25 patients completed the entire course of rhGM-CSF. Of the 16 patients who received ≥ 64 μg/M2/d for at least eight days, there were five patients who had an apparent rhGM-CSF response and 11 patients who did not respond. Of the parameters analyzed, only the number of CFU-GM progenitor cells infused per kilogram was significantly associated with an rhGM-CSF response. All patients receiving ≥ 1.2 x 104 CFU-GM progenitors per kilogram achieved an absolute neutrophil count (ANC) ≥ 1,000/μL by day 21 and had a > 50% decrement in ANC within 48 to 72 hours of discontinuing rhGM-CSF, as contrasted to none of the patients receiving ≤ 7.2 x 103 CFU-GM progenitors per kilogram. The number of CFU-GM progenitor cells infused per kilogram was significantly ($P < 0.001$) higher in the five patients demonstrating an accelerated neutrophil recovery as compared with the 11 patients without apparent rhGM-CSF benefit (median: 17.5 v 2.0 x 103/kg, respectively), although the number of total marrow cells infused was comparable in the two groups. These studies complement previous reports in demonstrating beneficial effects of **GM-CSF** on **autologous bone marrow** engraftment. Moreover, they highlight the need to preserve the CFU-GM content of the marrow in **autologous bone marrow** transplantation (ABMT) studies in which recombinant growth factors are being tested.

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ACCESSION NUMBER: 93008070 EMBASE
DOCUMENT NUMBER: 1993008070
TITLE: Granulocyte-macrophage colony-stimulating factor (**GM-CSF**): A variety of possible applications in clinical medicine.
AUTHOR: Weiss M.; Belohradsky B.H.
CORPORATE SOURCE: Abt Antimikrob Ther Infektionsimmuno, Universitats-Kinderklinik, Dr von Haunersches Kinderspital, Lindwurmstrasse 4,W-8000 Munchen 2, Germany
SOURCE: Infection, (1992) Vol. 20, No. SUPPL. 2, pp. S81-S83.
ISSN: 0300-8126 CODEN: IFTNAL
COUNTRY: Germany
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 930124
Last Updated on STN: 930124

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L28 ANSWER 1 OF 3 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004441259 EMBASE
TITLE: Angiogenic strategy for human ischemic heart disease: Brief overview.
AUTHOR: Fukuda S.; Yoshii S.; Kaga S.; Matsumoto M.; Kugiyama K.; Maulik N.
CORPORATE SOURCE: N. Maulik, Molecular Cardiology Laboratory, Department of Surgery, Univ. of Connecticut Medical School, Farmington, CT 06030-1110, Japan. nmaulik@neuron.uchc.edu
SOURCE: Molecular and Cellular Biochemistry, (2004) Vol. 264, No. 1-2, pp. 143-149.
Refs: 44
ISSN: 0300-8177 CODEN: MCBIB8
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20041104
Last Updated on STN: 20041104

AB In the Western World ischemic coronary disease is the leading cause of morbidity and mortality. Therapeutic approaches mostly aim to restore flow to a localized segment by angioplasty or bypass surgery. Therapeutic **angiogenesis** and or **arteriogenesis** describes a strategy where blood vessel formation is induced for the purposes of treating and/or preventing ischemic disease. At present, at least 17 clinical trials of myocardial **angiogenesis** have been presented involving over 900 patients. Therapeutic **angiogenesis** makes use of the administration of angiogenic growth factor protein or gene to promote the development of endogenous collateral vessels in ischemic myocardium. Most recently, interest has grown in the potential **angiogenesis** effects of cell therapy - such as **autologous bone marrow** cells or cultured stem cells - and there are now several groups initiating phase I/II trials in this area. .COPYRGT. 2004 Kluwer Academic Publishers.

L28 ANSWER 2 OF 3 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003009122 EMBASE
TITLE: [Cell transplants and gene therapy. New methods of teatment of post-infarction circulatory insufficiency]. PRZESZCZEPY KOMORKOWE I TERAPIA GENOWA. NOWE METODY LECZENIA POZAWAlOWEJ NIEWYDOLNOSCI KRAZENIA.
AUTHOR: Rozwadowska N.; Fiszer D.; Siminiak T.; Kalawski R.; Kurpisz M.
CORPORATE SOURCE: Prof. M. Kurpisz, Zaklad Genetyki Czlowieka Pan, ul. Strzeszynska 32, 60-479 Poznan, Poland. kurpimac@man.poznan.pl
SOURCE: Polski Przeglad Kardiologiczny, (2002) Vol. 4, No. 4, pp. 325-329.
Refs: 29
ISSN: 1507-5540 CODEN: PPKOAO
COUNTRY: Poland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
037 Drug Literature Index
LANGUAGE: Polish
SUMMARY LANGUAGE: Polish; English
ENTRY DATE: Entered STN: 20030116
Last Updated on STN: 20030116

AB The number of cases of post-infarction circulatory insufficiency is still on rise and presently employed forms of therapy do not directly access to the pathologically malformed tissue. The proposed, new therapeutic attempt is based on cellular engineering and gene therapy or combination of both. So far, there have been proposed **autologous bone marrow** cells, fibroblasts, myoblasts or kardiomyocytes as the source of tissue transplants to the post-infarction scar. Gene therapy is based upon administration of constructs containing genes connected with angiogenic process: VEGF (vascular endothelial growth factor), bFGF/FGF2 (basic fibroblast growth factor), PDGF-BB (platelet-derived growth factor) and HIF-1 alpha (**hypoxia** -inducible factor-1 alpha). As well cellular engineering as gene therapy were studied first in animal models. Majority of protocols were successful therefore phase I clinical trials began; at present even phase II clinical trials have been initiated. Collection of the data will allow to optimize a therapy and perhaps will deliver to patients and physicians a long awaited solution, i.e. successful treatment of increasing cases of post-infarction circulatory insufficiency. A present review summarizes new methods of treatment of post-infarcted heart.

L28 ANSWER 3 OF 3 EMBASE

ACCESSION NUMBER: 2000301751 EMBASE

TITLE: **Angiogenesis** induced by the implantation of self-bone marrow cells: A new material for therapeutic **angiogenesis**.

AUTHOR: Hamano K.; Li T.-S.; Kobayashi T.; Kobayashi S.; Matsuzaki M.; Esato K.

CORPORATE SOURCE: Dr. K. Hamano, First Department of Surgery, Yamaguchi Univ. School of Medicine, 1-1-1, Minamikogushi, Ube, Yamaguchi 755-8505, Japan. kimikazu@po.cc.yamaguchi-u.ac.jp

SOURCE: Cell Transplantation, (2000) Vol. 9, No. 3, pp. 439-443. Refs: 14
ISSN: 0963-6897 CODEN: CTRAE8

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology
025 Hematology
026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20000914
Last Updated on STN: 20000914

AB Bone marrow contains various primitive cells that are thought to secrete several angiogenic growth factors and may also differentiate into endothelial cells. The present study was conducted to investigate the possibility that bone marrow cells could be a novel material to induce **angiogenesis**. The expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) in rat bone marrow cells was examined by immunohistochemistry. The production of VEGF was compared in tissue culture supernatant under the conditions of normoxia and **hypoxia**. The process of **angiogenesis** that occurred following the implantation of bone marrow cells was determined using a rat cornea model. VEGF- and bFGF-positive cells were found in rat bone marrow. The production of VEGF from bone marrow cells was significantly more enhanced by **hypoxic** conditions than by normoxic conditions. The rat cornea model showed that bone marrow cell implantation created new vessels. The implantation of self-bone marrow cells is a novel and simple method of inducing **angiogenesis**.

=>

L33 ANSWER 1 OF 14 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 1999233208 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10218840
TITLE: Large scale recovery and characterization of stromal cell-associated primitive haemopoietic progenitor cells from filter-retained human bone marrow.
AUTHOR: Blazsek I; Delmas Marsalet B; Legras S; Marion S; Machover D; Misset J L
CORPORATE SOURCE: Institut du Cancer et d'Immunogenetique, Hopital Paul Brousse, Villejuif, France.
SOURCE: Bone marrow transplantation, (1999 Apr) 23 (7) 647-57. Journal code: 8702459. ISSN: 0268-3369.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990525
Last Updated on STN: 19990525
Entered Medline: 19990513

AB **Bone marrow aspirates** are composed of two cellular compartments, an abundant buffy coat suspension and a minor particulate fraction. The particulate fraction is routinely removed by filtration prior to transplantation in order to reduce the risk of embolism. This study shows that the filter-retained fraction includes many multicellular complexes, previously defined as haematons. A haematon is a finely arborized stromal-web which is tightly packed with haemopoietic progenitor cells and differentiated postmitotic cells. Comparison of the pooled buffy coat and the filter-retained materials from healthy donors showed that the haematon fraction contained 8-40 x 10(6) CD34+ cells, 20-115 x 10(3) high proliferative potential colony-forming cells (HPP-CFC) and 0.49-2.67 x 10(6) granulocyte-macrophage colony-forming unit (GM-CFU) which constituted 24+/-8% (10-36; n=8) of the total GM-CFU population harvested. Similar, but more variable recoveries of GM-CFU were obtained from the haematon fractions from patients with breast cancer (21+/-13%; n=10), Hodgkin's disease (33+/-19%; n=4), non-Hodgkin's lymphoma (21+/-18; n=7), but the recovery was lower from patients with acute myelogenous leukaemia (AML) (13+/-13%; n=6). The haematon fraction was enriched in CD34+ cells (2.5-fold), long-term culture initiating cells (LTC-IC/CAFC, week 5) (3.5-fold), HPP-CFC (2.8-fold) and GM-CFU (2.3-fold) over the buffy coat. Purified CD34+ cells expanded exponentially and produced 800 to 4000-fold more nucleated cells, 300 to 3500-fold more GM-CFU and 10 to 80-fold more HPP-CFC in stroma-free suspension culture with interleukin-1 (IL-1beta), IL-3, IL-6, **GM-CSF** and stem cell factor (SCF), than did the starting cell input. The haematon fraction produced significantly more progenitor cells than the buffy coat in long-term liquid culture (LTC). This was due to the higher frequency of LTC-IC/CAFC and to the presence of the whole spectrum of native, stroma cell-associated CAFC in haematons. Thus, the haematon includes the most productive haematogenous compartment in human BM. This simple enrichment strategy, using filter-retained haematons, provides a rational source of BM cells for large scale experimental and/or clinical studies on haemopoietic stem cells and on critical accessory stromal cells.

L33 ANSWER 2 OF 14 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999225044 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10210319
TITLE: Ex-vivo expansion of bone marrow progenitor cells for hematopoietic reconstitution following high-dose chemotherapy for breast cancer.
AUTHOR: Bachier C R; Gokmen E; Teale J; Lanzkron S; Childs C; Franklin W; Shpall E; Douville J; Weber S; Muller T; Armstrong D; LeMaistre C F
CORPORATE SOURCE: South Texas Cancer Institute, San Antonio 77229, USA.. cbachier@txdirect.net
SOURCE: Experimental hematology, (1999 Apr) 27 (4) 615-23.

Journal code: 0402313. ISSN: 0301-472X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990614

AB The use of hematopoietic growth factors, stromal monolayers, and frequent medium exchange allows the expansion of hematopoietic progenitors ex-vivo. We evaluated the use of ex-vivo expanded progenitor cells for hematopoietic reconstitution following high dose chemotherapy (HDC) in breast cancer patients. Patients with high-risk Stage II or metastatic breast carcinoma underwent **bone marrow aspirations** using general anesthesia. A total of 675-1125 x 10(6) mononuclear cells (MNC) were seeded for ex-vivo expansion for 12 days in controlled perfusion bioreactors (Aastrom Biosciences, Inc.). The bone marrow cultures, which included the stromal cells collected with the aspirate, were supplemented with erythropoietin, granulocyte-macrophage-colony stimulating factor (**GM-CSF**)/IL-3 fusion protein (PIXY 321), and flt3 ligand. Stem cell transplant was performed with expanded cells after HDC. A median bone marrow volume of 52.9 mL (range 42-187 mL) was needed to inoculate the bioreactors. Median fold expansion of nucleated cells (NC) and colony forming unit granulocyte-macrophage (CFU-GM) was 4.9 and 9.5, respectively. The median fold expansion of CD34+lin- and long-term culture-initiating culture (LTC-IC) was 0.42 and 0.32, respectively. Five patients were transplanted with ex-vivo expanded NC. Median days to an absolute neutrophil count > 500/microL was 18 (range 15-22). Median days to a platelet count > 20,000/microl was 23 (range 19-39). All patients had sustained engraftment of both neutrophils and platelets. Immune reconstitution was similar to that seen after HDC and conventional stem cell transplantation. We conclude that ex-vivo expansion of progenitor cells from perfusion cultures of small volume **bone marrow aspirates**, allows hematopoietic reconstitution after HDC.

L33 ANSWER 3 OF 14 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999038152 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9822358
TITLE: Effects of high dose medroxyprogesterone acetate on endogenous granulocyte macrophage-colony stimulating factor secretion and bone marrow cellularity in patients under cytotoxic chemotherapy.
AUTHOR: Aydin F; Demirkazik A; Icli F; Akbulut H; Samur M
CORPORATE SOURCE: Karadeniz Technical University, School of Medicine, Department of Internal Medicine, Trabzon, Turkey.
SOURCE: Journal of chemotherapy (Florence, Italy), (1998 Oct) 10 (5) 394-8.
Journal code: 8907348. ISSN: 1120-009X.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990209
Last Updated on STN: 19990209
Entered Medline: 19990122

AB Endogenous cytokine release and bone marrow cellularity of cancer patients receiving chemotherapy were investigated to elucidate the effect of high dose medroxyprogesterone acetate (MPA). MPA (1000 mg/day p.o.) was started after the first cycle of chemotherapy in patients with neutropenia. Administration of MPA was stopped a week after the second cycle of chemotherapy. Blood samples and **bone marrow aspirations** were obtained for granulocyte macrophage-colony stimulating factor (**GM-CSF**) assay one week after the

first and second cycles of chemotherapy. **GM-CSF** levels and bone marrow cellularities were compared before and after MPA treatment. Twelve of fifteen patients included in the study had a significant decrease in endogenous cytokine (**GM-CSF**) secretion after high dose MPA treatment. This result supports the hypothesis that decreased cytokine release leads to a decrease in myeloid progenitor cell proliferation and protects cells from the cytotoxic effects of chemotherapy. As a result of this protection, the myeloid cell population increases in bone marrow. No changes in erythrocytes and platelet counts were obtained.

L33 ANSWER 4 OF 14 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1998040271 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9374115
TITLE: The effect of treatment with budesonide or PGE2 in vitro on allergen-induced increases in canine bone marrow progenitors.
AUTHOR: Inman M D; Denburg J A; Ellis R; Dahlback M; O'Byrne P M
CORPORATE SOURCE: Asthma Research Group, McMaster University, Hamilton, Ontario, Canada.
SOURCE: American journal of respiratory cell and molecular biology, (1997 Nov) 17 (5) 634-41.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971209

AB Increased bone marrow granulocyte-macrophage colony forming units (GM-CFU) in dogs developing allergen-induced airway hyperresponsiveness can be accounted for by a factor(s) present in serum following the allergen challenge. The present study evaluated whether in vitro treatment of bone marrow with budesonide or prostaglandin (PG)E2, prevents allergen-induced bone marrow stimulation. Eight dogs were studied after allergen and diluent inhalation challenges. Budesonide (10[-7] M) or PGE2 (10[-6] M) was added to **bone marrow aspirated** 24 h after challenge. Budesonide or PGE2 was also added to **bone marrow aspirated** before challenge, to which serum taken 24 h after challenge was subsequently added. Non-adherent mononuclear bone marrow cells were incubated in the presence of the serum and granulocyte/macrophage colony stimulating factor (**GM-CSF**), granulocyte stimulating factor (G-CSF), or stem cell factor (SCF), and the number of GM-CFU counted. Allergen-induced increases in the number of GM-CFU in **bone marrow aspirated** 24 h after allergen ($P < 0.001$) were not attenuated by budesonide or PGE2 treatment ($P > 0.05$). However, GM-CFU increases in **bone marrow aspirated** before challenge and incubated with post-allergen challenge serum ($P < 0.001$) were blocked by either budesonide or PGE2 ($P < 0.001$). These findings demonstrate that budesonide and PGE2 can act directly on the bone marrow, preventing allergen-induced increases in inflammatory cell progenitor production. This suggests that the bone marrow must be considered as a possible site of action for drugs which attenuate allergen-induced asthmatic responses.

L33 ANSWER 5 OF 14 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 95399751 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7670096
TITLE: Results of a phase I/II trial of recombinant human granulocyte-macrophage colony-stimulating factor in very low birthweight neonates: significant induction of circulatory neutrophils, monocytes, platelets, and bone marrow neutrophils.
AUTHOR: Cairo M S; Christensen R; Sender L S; Ellis R; Rosenthal J; van de Ven C; Worcester C; Agosti J M
CORPORATE SOURCE: Children's Hospital of Orange County, CA 92668, USA.

SOURCE: Blood, (1995 Oct 1) 86 (7) 2509-15.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951026
Last Updated on STN: 19970203
Entered Medline: 19951019

AB Neonates, especially those of very low birthweight (VLBW), have an increased risk of nosocomial infections secondary to deficiencies in development. We previously demonstrated that granulocyte-macrophage colony-stimulating factor (**GM-CSF**) production and mRNA expression from stimulated neonatal mononuclear cells are significantly less than that from adult cells. Recombinant murine **GM-CSF** administration to neonatal rats has resulted in neutrophilia, increased neutrophil production, and increased survival of pups during experimental Staphylococcus aureus sepsis. In the present study, we sought to determine the safety and biologic response of recombinant human (rhu) **GM-CSF** in VLBW neonates. Twenty VLBW neonates (500 to 1,500 g), aged < 72 hours, were randomized to receive either placebo (n = 5) or rhuGM-CSF at 5.0 micrograms/kg once per day (n = 5), 5.0 micrograms/kg twice per day (n = 5), or 10 micrograms/kg once per day (n = 5) given via 2-hour intravenous infusion for 7 days. Complete blood counts, differential, and platelet counts were obtained, and tibial **bone marrow aspirate** was performed on day 8. Neutrophil C3bi receptor expression was measured at 0 and 24 hours. **GM-CSF** levels were measured by a sandwich enzyme-linked immunosorbent assay at 2, 4, 6, 12, and 24 hours after the first dose of rhuGM-CSF. At all doses, rhuGM-CSF was well tolerated, and there was no evidence of grade III or IV toxicity. Within 48 hours of administration, there was a significant increase in the circulating absolute neutrophil count (ANC) at 5.0 micrograms/kg twice per day and 10.0 micrograms/kg once per day, which continued for at least 24 hours after discontinuation of rhuGM-CSF. When the ANC was normalized for each patient's first ANC, there was a significant increase in the ANC on days 6 and 7 at each dose level. By day 7, all tested doses of rhuGM-CSF resulted in an increase in the absolute monocyte count (AMC) compared with placebo-treated neonates. In those receiving rhuGM-CSF 5.0 micrograms/kg twice per day, there was additionally a significant increase in the day 7 and 8 platelet count. Tibial **bone marrow aspirates** demonstrated a significant increase in the bone marrow neutrophil storage pool (BM NSP) at 5.0 micrograms/kg twice per day and 10.0 micrograms/kg once per day. Neutrophil C3bi receptor expression was significantly increased 24 hours after the first dose of rhuGM-CSF at 5.0 micrograms/kg once per day. The elimination half-life (T1/2) of rhuGM-CSF was 1.4 +/- 0.8 to 3.9 +/- 2.8 hours.(ABSTRACT TRUNCATED AT 400 WORDS)

L33 ANSWER 6 OF 14 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 92381704 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1380987
TITLE: Activation and differentiation of myelomonocytic cells in rheumatoid arthritis and healthy individuals--evidence for antagonistic in vitro regulation by interferon-gamma and tumor necrosis factor alpha, granulocyte monocyte colony stimulating factor and interleukin 1.
AUTHOR: Seitz M; Zwicker M; Pichler W; Gerber N
CORPORATE SOURCE: Division of Rheumatology, University Hospital, Inselspital, Bern, Switzerland.
SOURCE: Journal of rheumatology, (1992 Jul) 19 (7) 1038-44.
Journal code: 7501984. ISSN: 0315-162X.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19921018
Last Updated on STN: 19960129
Entered Medline: 19920925

AB We analyzed expression of HLA-DR and CD14 molecules on myelomonocytic cells and its regulation by various inflammatory cytokines in 6 patients with rheumatoid arthritis (RA) and 4 healthy individuals who had undergone **bone marrow aspiration**. At start of the bone marrow culture there was a significantly higher number of HLA-DR and CD14 positive bone marrow mononuclear cells in patients with RA than in normals. In addition, RA bone marrow mononuclear cells expressed an up to 10-fold higher mean density of both molecules than normal bone marrow mononuclear cells during the whole culture period of up to 14 days. The effect of the cytokines interferon-gamma (IFN-gamma), tumor necrosis factor alpha (TNF alpha), granulocyte monocyte colony stimulating factor (**GM-CSF**) and interleukin 1 (IL-1) on the expression of CD14 or HLA-DR was different: IFN-gamma strongly upregulated HLA-DR expression and down-regulated CD14 expression while TNF alpha, **GM -CSF** and IL-1 mainly stimulated CD14 expression on bone marrow mononuclear cells. Our data suggest that RA bone marrow mononuclear cells exhibit an activated phenotype and that TNF-alpha **GM-CSF** and IL-1 mainly stimulate the differentiation of bone marrow macrophages whereas IFN-gamma activates them.

L33 ANSWER 7 OF 14 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 93022880 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1405753
TITLE: Differentiation and maturation of growth factor expanded human hematopoietic progenitors assessed by multidimensional flow cytometry.
AUTHOR: Terstappen L W; Buescher S; Nguyen M; Reading C
CORPORATE SOURCE: Becton Dickinson Immunocytometry Systems, San Jose, CA 95131.
SOURCE: Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, U.K, (1992 Oct) 6 (10) 1001-10.
Journal code: 8704895. ISSN: 0887-6924.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921116

AB Non-adherent cord blood and bone marrow mononuclear cells were analyzed by multiparameter flow cytometry before and at day 2, 4, 7, and 11 of culture in recombinant interleukin 3 (IL-3) and granulocyte colony-stimulating factor (G-CSF, cord blood) or stem cell factor (SCF), IL3 and granulocyte-macrophage colony-stimulating factor (**GM-CSF** , BM) to assess the differentiation and maturational pathway of myeloid cells. Before cell culture cord blood contained progenitor cells (CD34+) in various differentiation stages (CD38(-)----CD38bright), mature lymphocytes, monocytes, and neutrophils, but no immature neutrophils and immature monocytes. During cell culture, all CD34+ cells acquired the CD38 antigen between day 2 and 5 of cell culture, the CD34 antigen was lost between day 5 and 11 of cell culture. Differentiation of cells into the myeloid cell lineage was characterized by the acquisition of both CD33 and CD71. The latter is indicative for the active proliferation of these cells. Maturation of the cells into the neutrophilic pathway was indicated by the acquisition of first the CD15 antigen followed by CD11b and CD16 respectively. Whereas maturation of the cells into the monocytic pathway was indicated by the acquisition of first CD11b followed by CD14 and a dim expression of both CD15 and CD16. In normal bone marrow, cells of various maturational stages are already present before cell culture. During cell culture differentiation of cells into the myeloid lineage and

maturation of the cells along the monocyte and neutrophilic lineage followed identical pathways as was observed before cell culture. Differentiation and maturational pathways of cord blood and adult bone marrow were identical. The results confirm the surface-antigen-defined pathways of myeloid cell differentiation described previously for non-cultured normal **bone marrow aspirates**.
The detailed assessment of cell maturation and differentiation of cultured cells by multidimensional flow cytometry permits the determination of the specific effects of various recombinant human growth factors on myeloid cells.

L33 ANSWER 8 OF 14 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 92331739 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1628706
TITLE: The effect of granulocyte-macrophage colony-stimulating factor on undifferentiated and mature acute myelogenous leukemia blast progenitors.
AUTHOR: Estrov Z; Park C H; Reading C L; Estey E H; Talpaz M; Kurzrock R; Deisseroth A B; Gutterman J U
CORPORATE SOURCE: Department of Clinical Immunology and Biological Therapy, University of Texas M.D. Anderson Cancer Center, Houston 77030.
SOURCE: Experimental hematology, (1992 Aug) 20 (7) 886-90.
Journal code: 0402313. ISSN: 0301-472X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920904
Last Updated on STN: 19920904
Entered Medline: 19920818
AB Granulocyte-macrophage colony-stimulating factor (**GM-CSF**) has been used recently to recruit undifferentiated acute myelogenous leukemia (AML) blasts into the S-phase of the cell cycle and increase the fraction of cells killed by cell cycle-specific drugs. Using three AML blast colony assays combined with a suspension culture (delta assay), we determined the in vitro effect of **GM-CSF** on mature and undifferentiated AML blast progenitors obtained from **bone marrow aspirates** of six AML patients. **GM-CSF** stimulated AML blast colony proliferation at a concentration of 5 ng/ml in the methylcellulose and the agar clonogenic assays in six of six AML marrow samples. However, in the delta assay, which selects for immature AML progenitors, **GM-CSF** did not affect AML blast colony-forming cells in five of six AML marrow samples at concentrations ranging from 5 to 300 ng/ml. Our data imply that **GM-CSF** stimulates mature but not undifferentiated AML blast progenitors. It is therefore possible that **GM-CSF** may not be beneficial as a recruiting agent in most AML patients.

L33 ANSWER 9 OF 14 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 91222649 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1827301
TITLE: Human granulocyte-macrophage colony-stimulating factor modulates in vitro growth in only a minority of continuous human tumour cell lines. EORTC Clonogenic Assay Screening Study Group.
AUTHOR: Anonymous
SOURCE: European journal of cancer (Oxford, England : 1990), (1991) 27 (3) 231-5.
Journal code: 9005373. ISSN: 0959-8049.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199106
ENTRY DATE: Entered STN: 19910630
Last Updated on STN: 19970203

Entered Medline: 19910612

AB Granulocyte-macrophage colony stimulating factor (**GM-CSF**) has potential usefulness in a range of clinical conditions, including the treatment of patients with myelosuppression induced by chemotherapy and/or radiotherapy. Prior to any extensive use of this material, however, assessment of its effects on non-haematopoietic tumour cell growth appeared warranted. Accordingly, five laboratories, all members of the EORTC Clonogenic Assay Screening Study Group, have monitored in vitro responses to **GM-CSF**, using their own individual assay procedures, in a series of 18 human tumour cell lines, predominantly of non-haematopoietic origin, 25 tumour biopsy specimens and samples from five normal **bone marrow aspirates**. Significant growth stimulation by **GM-CSF** addition was rare, being absent in all 25 "fresh" ovarian tumour samples tested, but was consistently observed in four of the 18 continuous tumour cell lines tested (1 breast and 3 ovary) and all five normal **bone marrow aspirates**.

L33 ANSWER 10 OF 14 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 91147580 EMBASE
DOCUMENT NUMBER: 1991147580
TITLE: Human granulocyte-macrophage colony-stimulating factor modulates in vitro growth in only a minority of continuous human tumour cell lines.
AUTHOR: Aapro M.S.; Charrin C.; Krauer F.; Delaloye J.F.; Dietal M.; Hill B.T.; Hosking L.K.; Merlin J.L.; Ramacci C.; Weber B.; Silvestro L.; Viano I.
CORPORATE SOURCE: Division of Oncology, University Hospital, Geneva, Switzerland
SOURCE: European Journal of Cancer, (1991) Vol. 27, No. 3, pp. 231-235.
ISSN: 0277-5379 CODEN: EJCAEL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911216
Last Updated on STN: 911216

AB Granulocyte-macrophage colony stimulating factor (**GM-CSF**) has potential usefulness in a range of clinical conditions, including the treatment of patients with myelosuppression induced by chemotherapy and/or radiotherapy. Prior to any extensive use of this material, however, assessment of its effects on non-haematopoietic tumour cell growth appeared warranted. Accordingly, five laboratories, all members of the EORTC Clonogenic Assay Screening Study Group, have monitored in vitro responses to **GM-CSF**, using their own individual assay procedures, in a series of 18 human tumour cell lines, predominantly of non-haematopoietic origin, 25 tumour biopsy specimens and samples from five normal **bone marrow aspirates**. Significant growth stimulation by **GM-CSF** addition was rare, being absent in all 25 'fresh' ovarian tumour samples tested, but was consistently observed in four of the 18 continuous tumour cell lines tested (1 breast and 3 ovary) and all five normal **bone marrow aspirates**.

L33 ANSWER 11 OF 14 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 91091207 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2265109
TITLE: Interleukin-6 is a cofactor for the growth of myeloid cells from human **bone marrow aspirates** but does not affect the clonogenicity of myeloma cells in vitro.
AUTHOR: Borinaga A M; Millar B C; Bell J B; Joffe J K; Millar J L;

Gooding R; Riches P; McElwain T J
CORPORATE SOURCE: Section of Medicine, Institute of Cancer Research, Sutton, Surrey.
SOURCE: British journal of haematology, (1990 Dec) 76 (4) 476-83. Journal code: 0372544. ISSN: 0007-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910322
Last Updated on STN: 19970203
Entered Medline: 19910213

AB Several groups have claimed that IL-6 is a growth factor for human myeloma cells in vitro. **Bone marrow aspirates** from 30 patients at different stages of treatment with VAMP/high dose melphalan, were examined for myeloma colony formation (MY-CFUc) using a clonogenic assay in vitro. Myeloma cells from 16/30 patients produced MY-CFUc in our assay system, which uses heavily irradiated HL60 cells as an underlay in soft agar. These heavily irradiated cells were shown to be essential for the inhibition of granulocyte-macrophage colonies (GM-CFUc). The addition of recombinant human IL-6 (10 ng/plate) reduced the number of bone marrow samples which produced MY-CFUc from 16 to six. Furthermore, the addition of antibody to IL-6 (1 microgram/plate) failed to inhibit MY-CFUc from 6/7 samples. Conditioned medium from human peripheral blood mononuclear cells (PBMC-CM) contains approximately 2 ng/ml IL-6 and can be used to stimulate the growth and maintenance of the B9 murine IL-6 dependent hybridoma cell line. Recombinant human IL-6 supported the growth of B9 cells in a clonogenic assay and growth was inhibited by anti-IL-6 in the presence of rhIL-6 or PBMC-CM. Mononuclear cells from a second group of myeloma patients were cultured in soft agar in a mixture of PBMC-CM and fresh growth medium. Nine of the 10 samples produced myeloid colonies which consisted of granulocytes, monocytes and macrophages and the number of colonies was reduced by at least 50% in 6/8 samples when anti-IL-6 was added to the cultures. In no instance were MY-CFUc produced. Also, conditioned medium from the bladder carcinoma cell line 5637, which is used routinely as a source of granulocyte-macrophage colony stimulating factor (**GM-CSF**), contains approximately 4 ng/ml IL-6. Although rhIL-6 failed to stimulate GM-CFUc in the absence of other growth factors, addition of anti-IL-6 to cultures containing a suboptimal amount of 5637-CM reduced the number of colonies by 50%. These data provide evidence that IL-6 is a cofactor for the growth of myeloid precursors but does not affect the proliferation of human myeloma cells in vitro.

L33 ANSWER 12 OF 14 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 90214773 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2182330
TITLE: Hematon, a multicellular functional unit in normal human bone marrow: structural organization, hemopoietic activity, and its relationship to myelodysplasia and myeloid leukemias.
AUTHOR: Blazsek I; Misset J L; Benavides M; Comisso M; Ribaud P; Mathe G
CORPORATE SOURCE: Institut du Cancer et d'Immunogenetique, Universite Paris-Sud, France.
SOURCE: Experimental hematology, (1990 May) 18 (4) 259-65. Journal code: 0402313. ISSN: 0301-472X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900622
Last Updated on STN: 19900622
Entered Medline: 19900517

AB An increasing amount of data provides strong evidence for the complex multifactorial control of primary hemopoietic functions. Here we present

a new multicellular functional unit, the Hematon, isolated from the light-density floating fraction of normal human **bone marrow** (BM) **aspirates**. The Hematon is organized in a compact, three-dimensional spheroid complex from central adipocytes, fibroblastoid cells, and resident macrophages that compartmentalize myeloid, erythroid, and megakaryocyte progenitor cells and their progenies. The Hematon fraction is more than twofold more abundant in progenitor cells when compared to the mononuclear cell (MNC) fraction as gauged by cytological techniques and by analysis of granulocyte-macrophage colony-forming unit (GM-CFU) populations. Individual Hematons may produce, within 2-3 weeks, up to 50,000 hemopoietic cells of different cell lineages in organotypic microcultures. Recombinant human hematopoietic growth factors interleukin 3 (IL-3), granulocyte-macrophage colony-stimulating factor (**GM-CSF**), granulocyte colony-stimulating factor (G-CSF), and macrophage colony-stimulating factor (M-CSF) significantly stimulated the endogenous cell production of some but not all of the individually treated Hematons, indicating the heterogeneity of factor-responsive cells within the Hematon population. Comparative observations of 184 BM aspirates support the hypothesis that the presence of Hematons in a BM aspirate correlates positively with homeostatic blood cell production, because the Hematon was present in normal BM (31/40) and it was rare among patients with myelodysplastic syndromes (15/53), acute myeloblastic leukemia (7/39), and chronic myelocytic leukemia (5/52). We suggest that the Hematon represents a unifying model around which the variability of fundamental BM functions and dysfunctions can be explored.

L33 ANSWER 13 OF 14 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 90071371 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2480049
TITLE: Effects of recombinant human G-CSF and **GM-CSF** on primary human leukemic cells.
AUTHOR: Itoh K; Bessho M; Hirashima K
SOURCE: Nippon Ketsueki Gakkai zasshi : journal of Japan Haematological Society, (1989 Sep) 52 (6) 988-95. Journal code: 2984803R. ISSN: 0001-5806.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199001
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19900111

AB The effects of recombinant human granulocyte colony-stimulating factor (rhG-CSF) and recombinant human granulocyte-macrophage colony-stimulating factor (rhGM-CSF) on primary human leukemic cells were studied. Phagocyte-depleted mononuclear cells containing more than 88% blasts were obtained from peripheral blood of 11 AML and 2 ALL patients and from **bone marrow aspirates** from 2 ALL patients. The leukemic cells were incubated with these CSF in suspension cultures or in methylcellulose cultures. In suspension cultures, the spontaneous proliferation was observed in 1 M4 patient. RhG-CSF stimulated the leukemic cell proliferation in 5 AML, cases and rhGM-CSF that in 4 AML cases. In methylcellulose cultures, spontaneous colony formation occurred in 3 M4 patients. RhG-CSF and rhGM-CSF stimulated the leukemic colony formation in 8 AML cases. The CSFs had an additive effect in both cultures. Neither CSF induced O2- production or phagocytic activity. From these results, we concluded that both CSFs stimulated the proliferation of leukemic cells without inducing differentiation.

L33 ANSWER 14 OF 14 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 90028115 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2478185
TITLE: Isolation of human megakaryocytes by immunomagnetic beads.
AUTHOR: Tanaka H; Ishida Y; Kaneko T; Matsumoto N
CORPORATE SOURCE: Third Department of Internal Medicine, Yamaguchi University, School of Medicine, Ube, Japan.

SOURCE: British journal of haematology, (1989 Sep) 73 (1) 18-22.
Journal code: 0372544. ISSN: 0007-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198912
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19960129
Entered Medline: 19891205

AB A simple method was developed to purify human megakaryocytes to homogeneity from normal **bone marrow aspirates** . An initial separation of marrow between 1.020 and 1.050 g/ml. Percoll density cut was used to enrich megakaryocytes. After washing, the cells were suspended with immunomagnetic beads which were coated with sheep anti-mouse IgG antibody and treated with anti-human glycoprotein (GP) IIb/IIIa monoclonal antibody, or the cells were treated with human platelet GP IIb/IIIa monoclonal antibody and suspended with the immunomagnetic beads which were coated with sheep anti-mouse IgG antibody. Megakaryocytes were selectively separated using a magnet. All of the isolated cells were morphologically recognizable megakaryocytes. 1.5-3.1 x 10(4) megakaryocytes were obtained from 1.7-4.5 x 10(8) bone marrow nuleated cells. These cells were all positive in immunoenzymatic staining for GP IIb/IIIa. Megakaryocytes obtained by this method responded to recombinant human **GM-CSF** (rhGM-CSF) showing an increased 3H-thymidine (3H-dT) incorporation. These data show that this method is useful for obtaining pure megakaryocyte populations which can be submitted to comprehensive biological studies.

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